will improve survival in children with high-risk solid tumors. Fifteen patients were enrolled from March 2000 to August 2004 with a median age of 6 years (2–19). Each had received at least 2 courses of chemotherapy prior to study enrollment. Patients (Table 1) had the following diagnoses: recurrent Wilms tumor (n = 5), high-risk Ewing's sarcoma (n = 3), recurrent hepatoblastoma (n = 2), recurrent retinoblastoma (n = 2), recurrent germ cell tumor (n = 2), and undifferentiated sarcoma (n = 1). Patients were prepared with etoposide (800 mg/m^2/day on −6, −5, −4), carboplatin (667 mg/m^2/day on −6, −5, −4), and cyclophosphamide (1800 mg/m^2/day on −3, −2) prior to the first transplant, and melphalan (60 mg/m^2/day on −8, −7, −6) and cyclophosphamide (500 mg/m^2/day on −5, −4, −3, −2) prior to the second. Children received a median of 3.86 × 10^8 TNC/Kg (2.3–9.4) prior to the first transplant, and 4.1 × 10^8 (2.5–10.5) TNC/Kg prior to the second. Eight patients were in complete remission and 7 were in partial remission at the time of first transplant. One patient received local radiation instead of the second transplant due to parental preference. Following each rescue, patients achieved an ANC > 500 at a median of 13 days (11–34) and 12 days (10–31), respectively. Patients achieved a platelet count >20,000 at a median of 22 days (13–37) and 37 days (15–113), respectively. There was a median of 38 days between rescues (29–49). Five patients received radiation therapy post-transplant to relapse sites. There were no toxic deaths. Toxicity was primarily hematopoietic. Nine of 15 are surviving, 2 with recurrent disease following tandem therapy at a median follow-up of 22 months (11–55). Relapses following transplant occurred at the primary site (n = 3), distant (n = 3), and primary/distant (n = 2). Five have died from progressive disease; 1 from late pulmonary toxicity. We conclude that tandem stem cell transplant used as consolidation in patients with solid tumors is feasible, well tolerated, and offers the potential for cure in some patients with high-risk disease (Table1).

Table 1. *Patient Characteristics*

Patient	Diagnosis	Stage/ Location	Relapse Site Prior to SCT	Relapse Site Following SCT	Follow-up Post Transplant
1	Undifferentiated sarcoma	Pelvis			NED, 55 months
2	Ewing's	Pelvis		Primary site, lungs	PD, died - 39 months
3	Hepatoblastoma	Stage IV		Primary site	Alive, stable disease - 53 months
4	Wilms	Recurrent stage IV	Primary site, lungs		NED, 45 months
5	Ewing's	Pelvis		Primary site, lungs	PD, died - 11 months
6	Wilms	Recurrent stage I	Liver		NED, 49 months
7	Wilms	Recurrent stage III	Lungs	CNS	Alive, stable disease - 38 months
8	Ewing's	Metastatic			NED, 41 months
9	Hepatoblastoma	Recurrent stage IV	Primary site	Lungs	PD, died - 22 months
10	Germ cell tumor	Stage IV			Pulmonary toxicity, died - 19 months
11	Wilms	Recurrent stage II	Primary site	Primary site	NED, 27 months
12	Wilms	Recurrent stage III	Primary site	Primary site	PD, died - 12 months
13	Retinoblastoma	Bilateral	Sinus, orbit		NED, 16 months
14	Retinoblastoma	Bilateral	Pineal	Pineal	PD, died - 11 months
15	Germ cell tumor	Pineal	Primary site		NED, 13 months

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PHARMACOKINETICS (PK) OF 2 DOSING REGIMENS OF PALIFERMIN IN PATIENTS (Pts) WITH HEMATOLOGIC MALIGNANCIES (HM) UNDERGOING HIGH-DOSE CHEMORADIOTHERAPY AND HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

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For patients (pts) with HM undergoing HSCT, oral mucositis (OM) is a frequent and debilitating complication that negatively impacts treatment outcomes, patient quality of life, and healthcare resources. Palifermin reduces the incidence and duration of severe OM in the HSCT setting. This phase 1 open-label study assessed the PK of 2 palifermin dosing regimens. **Methods:** Pts were 18 to 76 years old with HM and a Karnofsky performance score ≥70%. Palifermin was administered intravenously once daily as follows: 60 mcg/kg/day for 3 consecutive days on day −11, day −10, and day −9 before conditioning (total body irradiation [TBI] + etoposide + cyclophosphamide) and following HSCT on days 0, 1, and 2 (part A) and a single dose of 180 mcg/kg (part B) before conditioning on day −11 and after HSCT on d 0. In part A (6 total doses), PK parameters were assessed after the first, third, fourth, and sixth doses. In part B (2 total doses), assessments were made after each dose administration (day −11 and day 0). **Results:** In part A, 13 pts received palifermin; in part B, 12 pts received the single dose on day −11 and 11 pts received the single dose on day 0. For both dosing regimens, palifermin concentrations declined rapidly (≥98% decrease) in the first 30 minutes postdose, followed by a slight increase in mean concentrations between 1 and 4 hours and then a terminal decay phase. Respective mean (SD) PK parameter values for the 2 dosing regimens are shown in Table 1. In part A, mean $AUC_{0\text{-}t}$ values were comparable between doses 1 and 3 (within 15%) and 1 and 4 (within 1%). In part B, mean PK parameter values were similar (within 10% of each other) between doses 1 and 2. The mean AUC after the first 180 mcg/kg dose in part B was approximately 4-fold higher than that after the first 60 mcg/kg dose in part A. Mean half-life values ranged between 3.3 to 5.7 hours in part A and the value was 5.4 hours in part B. **Conclusions:** The PK data in pts receiving HSCT were consistent with approximately dose-linear PK in the dose range of 60 and 180 mcg/kg, with no observed accumulation, based on AUC, after 3 daily doses of 60 mcg/kg in this pt population in the HSCT setting (Table1).

Table 1.

Dosing Regimen (Dosing Day)	n	$AUC_{0\text{-}t}$ (hr × ng/mL) Mean (SD)	Clearance (mL/hr/kg) Mean (SD)	V_{ss} (mL/kg) Mean (SD)
Part A - 60 mcg/kg/day × 3 consecutive days				
1st dose (day −11)	9 to 13	34.3 (15.9)	1730a (497)	5320a (2330)
3rd dose (day −9)	13	39.8 (36.4)	-	-
4th dose (day 0)	11 to 13	34.8 (22.5)	2030a (862)	3870a (2080)
6th dose (day 2)	13	21.2 (15.1)	-	-
Part B - 180 mcg/kg/day × 1 day				
1st dose (day −11)	12	140 (50.9)	1460 (600)	4290 (3270)
2nd dose (day 0)	11	143 (71.8)	1770 (1290)	4270 (4700)

Accurate computations of clearance (CL) and volume of distribution at steady state (V_{ss}) were not possible for some concentration-time profiles.

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THE FAILURE OF PROGNOSTIC MODELS (PM) FOR HODGKINS DISEASE (HD) TO PREDICT OUTCOMES AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT)

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PM have been developed for patients with advanced HD in an effort to identify high-risk individuals for and predict outcomes of ASCT. Four PM were evaluated in patients transplanted in our program between 1993 and 2005. One hundred and thirteen patients with relapsed or refractory HD received ASCT. Forty-five patients received a conditioning regimen of busulfan, melphalan, and thiotepa (BuMelTT), whereas 68 patients received other standard conditioning regimens (SCR) including Cy/TBI/VP (23), CBV (39), and other (6). Followup is 113 weeks for BuMelTT

patients and 201 weeks for SCR patients. Factors differentiating the BuMelTT and SCR groups included median followup post-ASCT, total percent relapse after transplant, death after transplant, relapse in prior radiation field, and stage at salvage therapy pre-ASCT. To date, 37% of the BuMelTT and 56% of SCR patients have relapsed ($P < .05$) with a median time to relapse of 30 and 36 weeks (P = NS), respectively. Median OS, EFS, and RFS have not yet been reached for BuMelTT patients compared with 439 (P = .03), 67 (P = NS), and 74 (P = NS) weeks for the SCR patients respectively. TRM was 5% in both groups at 5 years. Secondary myelodysplasia has been seen in one patient transplanted with BuMelTT and one with SCR. In multivariate analysis the BuMelTT regimen and chemosensitive disease were associated with improved OS (HR = 0.19 and 0.31, respectively). Relapse in prior radiation field predicted for poor EFS and OS (HR = 3.43). We investigated the predictive value of 4 PM on the entire group, BuMelTT and SCR cohorts. Each of these models has identified 3 poor prognostic indicators on the basis of multivariate analysis. Patients with 0 or 1 factor were considered good risk and 2 or 3 factors poor risk. Only the SWOG model was predictive for OS for the entire group ($P < .01$) and for the BuMelTT (P=0.05) and SCR ($P < .01$) cohorts. The SWOG model was also able to differentiate EFS between good and poor risk patients for the entire group (P = .02) and SCR group (P = .05) but not for the BuMelTT cohort. None of the models could differentiate between good and poor risk patients with regard to RFS. When good and poor risk was defined as 0 factors versus 1 to 3 factors, the RPCI model was predictive of OS (P = .02) and EFS (P = .02) but only for the BuMelTT cohort. The PM evaluated had limited utility in our patient cohort with only the SWOG model being predictive of outcome. Large multi-institutional studies are needed to improve PM for transplantation in advanced HD.

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PACLITAXEL FOLLOWED BY FILGRASTIM FOR PERIPHERAL BLOOD STEM CELL (PBSC) MOBILIZATION IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES WHO EXPERIENCED PRIOR MOBILIZATION FAILURES

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Cyclophosphamide followed by filgrastim (G-CSF) is frequently utilized for PBSC mobilization in patients with hematologic malignancies, but is associated with adverse events such as hemorrhagic cystitis and a rate of febrile neutropenia as high as 30%. In addition, white blood cell recovery varies among patients making it difficult to predict when to initiate apheresis. Our institution previously reported the efficacy of paclitaxel followed by G-CSF for PBSC mobilization in 30 patients with hematologic malignancies. In 86% of those patients, paclitaxel mobilization was the initial mobilization attempt. We report our experience with paclitaxel 250 mg/m^2 IV once followed by G-CSF 10-16 mcg/kg/day in 27 consecutive patients treated at Audie L. Murphy Memorial Veterans Hospital between 1/98 and 9/05. Twenty-one (78%) failed mobilization with G-CSF 16 mcg/kg/day alone, 5 (18%) failed mobilization with cyclophosphamide 3 g/m^2 followed by G-CSF, and 1 (4%) failed mobilization with rituximab, ifosfamide, carboplatin, and etoposide followed by G-CSF. Eight patients had multiple myeloma (MM), 17 had non-hodgkin's lymphoma, and 2 had acute myelogenous leukemia. Similar to our prior experience, 74% of patients began apheresis on day 8 after paclitaxel administration, based on a rising peripheral white blood cell count. The remaining patients began apheresis on day 9 or 10 after paclitaxel administration. Eighteen (67%) of 27 patients collected the target number of CD34+cells, defined as 2×10^6 cells/kg. An additional 4 patients underwent PBSC transplant with fewer than 2×10^6 CD34+ cells/kg (median 1.83, range 1.43&ndsh;1.98). One patient successfully collected adequate PBSC but elected to undergo allogeneic PBSC transplant; thus 21 (78%) of 27 patients proceeded to high-dose chemotherapy followed by autologous PBSC transplant. Median neutrophil (ANC $> 0.5 \times 10^9$/L) and platelet (platelet20×10^9/L) recovery was 11 days (range 8–12) and 13 days (range 9–24), respectively. Three patients (11%) developed febrile neutropenia following paclitaxel resulting in one death prior to high-dose chemotherapy in a patient with MM. **Conclusions:** Paclitaxel followed by G-CSF is an effective mobilization strategy for patients with hematologic malignancies who failed to mobilize PBSC with other mobilization regimens. The low incidence of febrile neutropenia and the predictable kinetics of white blood cell recovery make this combination an attractive alternative for patients who fail to mobilize PBSC.

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HIGH-DOSE CHEMOTHERAPY (HDCT) WITH HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) IN PATIENTS WITH POOR PROGNOSIS EWING FAMILY TUMORS (EFT)

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Objective: To evaluate the feasibility and safety of treatment with two cycles of HDCT followed by autologous HSCT in patients (pts) with poor prognosis EFT. A retrospective analysis included 20 EFT pts treated at City of Hope National Medical Center with 2 cycles of HDCT and HSCT from 1997 to 2003. HDCT for the first cycle consisted of melphalan (MEL)/carboplatin (CARB) in 9 pts and Mel/busulfan (BU) in 11 pts. HDT for the second cycle consisted of MEL/CARB (n = 5); MEL/BU (n = 3); and cyclophosphamide/etoposide/CARB (n = 5). A descriptive analysis of the safety, rate of recurrence, transplant-related morbidity (TRM) and mortality, event-free survival (EFS), and overall survival (OS) are reported. **Results:** Out of 20 eligible patients, 13 (65%) received 2 cycles of HDCT followed by autologous HSCT. Seven (35%) patients did not proceed to a second cycle as planned: 2 (28.5%) patients refused, 2 (28.5%) patients died of rapidly progressive disease, 1 (14%) patient died of idiopathic pulmonary fibrosis, 1 (14%) patient had previous radiation, and 1 (14%) patient had renal failure. The median follow-up (n = 20) was 2.4 years (range 0.1–7.8 years). Grade 4 adverse events were limited to mucositis and pancytopenia. No TRM was recorded after the first cycle of HDT and HSCT. There was one death after second cycle due to rapidly progressive disease. A sustained absolute neutrophil count (ANC $> 1000/mm^3$) for both cycles was achieved at the median of 11 days. A sustained platelet count ($>50{,}000/mm^3$) was achieved at a median of 17 to 20 days. There were no differences in OS rates between various HDCT regimens used and between patients with or without metastatic disease disease at the time of diagnosis. The Kaplan-Meier estimates of OS and EFS at three years were 45% (CI 0.22, 0.69) and 47% (CI 0.25,0.70), respectively. For patients who have received two cycles of HDCT followed by HSCT, the Kaplan-Meier estimates of OS and EFS at 3 years were 58% (CI 0.30, 0.86) and 58% (CI 0.30, 0.86), respectively. **Conclusions:** Dose-intensification with two cycles of HDCT and HSCT is feasible and relatively safe, with low and acceptable treatment related morbidity and mortality. Adding a second course of therapy does not impair engraftment. Both OS and EFS compare favorably with previously published reports. HDCT with HSCT may improve outcome in patients with poor prognosis EFT. Further studies are required to establish the optimal regimen for HDCT.

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A LONG-TERM EXPERIENCE USING AUTOLOGOUS STEM CELL TRANSPLANTATION FOR THE MANAGMENT OF HODGKIN'S LYMPHOMA

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Hodgkin's disease (HD) patients generally have a good long-term prognosis with approximately 70% cure rate. However, the prognosis significantly declines after disease relapse. High-dose chemotherapy with autologous stem cell transplantation is an effective salvage option for patients in relapse with 5-year OS of 50%, and has become an accepted therapy. While transplantation